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Protein translocation through anthrax toxin channels formed in planar lipid bilayers.

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The 63-kDa fragment of the protective antigen (PA) component of anthrax toxin forms a heptameric channel, (PA63)7, in acidic endosomal membranes that leads to the translocation of edema factor (EF) and lethal factor (LF) to the cytosol. It also forms a channel in planar phospholipid bilayer membranes. What role does this channel play in the translocation of EF and LF? We report that after the 263-residue N-terminal piece of LF (LFN) binds to its receptor on the (PA63)7 channel and its N-terminal end enters the channel at small positive voltages to block it, LFN is translocated through the channel to the opposite side at large positive voltages, thereby unblocking it. Thus, all of the translocation machinery is contained in the (PA63)7 channel, and translocation does not require any cellular proteins. The kinetics of this translocation are S-shaped, voltage-dependent, and occur on a timescale of seconds. We suggest that the translocation process might be explained simply by electrophoresis of unfolded LFN through the channel, but the refolding of the N-terminal half of LFN as it emerges from the channel may also provide energy for moving the rest of the molecule through the channel.

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